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CURRENT STATUS OF IMMUNOGLOBULIN M AND IMMUNOGLOBULIN G SEROPREVALENCE OF TORCH INFECTIONS IN PREGNANT WOMEN WITH BAD OBSTETRIC HISTORY AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: TORCH stands for Toxoplasma gondii, Rubella virus, Cytomegalo virus (CMV) and Herpes simplex virus-2 (HSV-2). These infections are transmitted to the foetus through transplacental route at any time during gestation or sometimes at the time of delivery. The infection may be asymptomatic or mild in mother but associated with inadvertent outcomes for the foetus. One of the causes of BOH is maternal infection. TORCH infection is asymptomatic in pregnant women and on clinical basis it is difficult to diagnose. **Aim:** To study the TORCH infection (IgM and IgG antibodies) prevalence in pregnant women with Bad Obstetric History. **Materials And Methods:** A hospital based cross-sectional study conducted in Department of Microbiology in collaboration with Department of Obstetrics and Gynecology, SHKM GMC, Nalhar, Nuh, Haryana over a period of one year (February 2020 - January 2021). A total of 90 samples were included in the study including control group. **Results:** The IgM seroprevalence of TORCH in participants with bad obstetric history was found to be 11.11%. In cases with Bad obstetric history prevalence of IgM Toxoplasma, Rubella, Cytomegalovirus & Herpes Simplex Virus was found as 4.44%, 0%, 2.22% & 4.44% respectively and prevalence of IgG Toxoplasma, Rubella, Cytomegalovirus, & Herpes Simplex Virus was found as 53.33%, 91.11%, 88.89% & 66.67% respectively. **Conclusion:** This study concluded that a previous history of pregnancy wastage and the serological screening for TORCH infections during current pregnancy must be considered while managing BOH cases to reduce the adverse fetal outcome.

INTRODUCTION

In 1971 Andres Nahmias proposed the acronym TORCH to highlight a group of agents which cause congenital and perinatal infections. TORCH stands for Toxoplasma gondii, Rubella virus, Cytomegalo virus (CMV) and Herpes simplex virus-2 (HSV-2). These infections are transmitted to the foetus through transplacental route at any time during gestation or sometime at the time of delivery.[1] The infection can be asymptomatic or with mild symptoms in mother but associated with inadvertent outcomes for the foetus.[2]

Bad obstetric history (BOH) is defined as pregnancy outcomes in terms of two or more consecutive spontaneous abortions, still births, intrauterine growth retardation, history of intrauterine fetal death, early neonatal death and/or congenital anomalies. One of the cause of BOH is maternal infection. Other causes may be genetic, hormonal, abnormal maternal immune response.[1,3,4]

TORCH infection is asymptomatic in pregnant women and on clinical basis it is difficult to diagnose. In pregnant women the diagnosis of acute TORCH infection is established by either demonstration of seroconversion of paired sera or by demonstration of specific IgM antibodies[3,8].

Rising titres of IgG (4 to 8-fold) in serum samples taken 2 weeks apart, indicates a recent infection.[5] Enzyme linked immunosorbent assay (ELISA) for IgM is highly sensitive and specific for screening TORCH infections .[3,4,6] TORCH screening in antenatal period helps to identify high risk mothers and their developing foetus who are at increasing risk of complications during /after pregnancy.[2]

The prevalence of TORCH infection varies geographically.[3,4,5,6] To the best of our knowledge, baseline data on seropositivity is not available from this part of Haryana.

Therefore, the present study was undertaken to study seroprevalence of TORCH infection and to know the exact etiological agent in pregnant women with bad obstetric history.

Methodology

This was a hospital based cross-sectional study conducted in the Department of Microbiology in collaboration with Department of Obstetrics and Gynecology, SHKM GMC, Nalhar, Nuh, Haryana, for the duration of 1 year (February 2020 to January 2021).

A total of 90 samples were collected from pregnant women including 45 cases with BOH and 45 controls without BOH. Cases were included in the study group depending on previous history of having two or more consecutive spontaneous abortions, still births, intrauterine growth retardation, history of intrauterine fetal death, early neonatal death and/or congenital anomalies.

Details of patients such as name, age, sex, occupation, educational status, provisional diagnosis, history of consanguinity, socioeconomic status, previous obstetric history and medical history of pregnant women were noted. 5 ml of blood sample was collected after obtaining written informed consent.

The serum was then separated and stored at -20 ^{0} C. IgG and IgM were detected by Enzyme Linked Immuno Assay (ELISA). Samples were processed along with positive and negative controls. ELISA was performed as per literature available with the kit. Kit used were of XEMA company.

RESULTS

As depicted in figure 1, we had equal number 45 (50%) of participants with good and bad obstetric history.

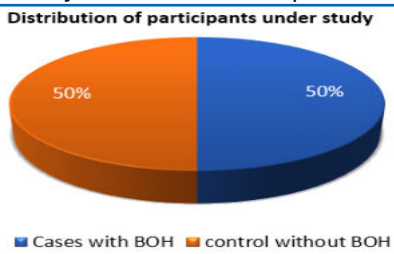

Figure 1: Distribution of TORCH participants under study.

Results revealed that of the total 45 cases, 11.1% were TORCH IgM seropositive while among controls none were seropositive. Among them 4.44% were positive for Toxoplasma, 0% for Rubella, 2.22% for CMV and 4.44% for HSV TORCH agents. The prevalence of IgG Toxoplasma, Rubella, Cytomegalovirus, & Herpes Simplex Virus was found as 53.33%, 91.11%, 88.89% & 66.67% in cases with BOH. In control group IgG Toxoplasma, Rubella, CMV, HSV was found in 48.89%, 86.67%, 97.78 & 75.56%.

Table 1: -Comparison of TORCH infection between good and bad obstetric history.

TORCH	Good obstetric history (n=45) (controls)	Bad obstetric history (n=45) (cases)	Total	P value
Toxoplasma IgM				
Negative	45 (100%)	43 (95.56%)	88 (97.78%)	0.494 †
Positive	0 (0%)	2 (4.44%)	26 (2.22%)	
Toxoplasma IgG				
Negative	23 (51.11%)	21 (46.67%)	44 (48.89%)	0.673 ‡
Positive	22 (48.89%)	24 (53.33%)	46 (51.11%)	
Syphilis				
Non-reactive	45 (100%)	45 (100%)	90 (100%)	No p value
Rubella IgM				
Negative	45 (100%)	45 (100%)	90 (100%)	No p value
Rubella IgG				
Negative	6 (13.33%)	4 (8.89%)	10 (11.11%)	0.739 †
Positive	39 (86.67%)	41 (91.11%)	80 (88.89%)	
Cytomegalo virus IgM				
Negative	45 (100%)	44 (97.78%)	89 (98.89%)	1†
Positive	0 (0%)	1 (2.22%)	1 (1.11%)	
Cytomegalo virus IgG				
Negative	1 (2.22%)	5 (11.11%)	6 (6.67%)	0.203 †
Positive	44 (97.78%)	40 (88.89%)	84 (93.33%)	
Herpes simplex virus IgM				
Negative	45 (100%)	43 (95.56%)	88 (97.78%)	0.494 †
Positive	0 (0%)	2 (4.44%)	2 (2.22%)	
Herpes simplex virus IgG				
Negative	11 (24.44%)	15 (33.33%)	26 (28.89%)	0.352 ‡
Positive	34 (75.56%)	30 (66.67%)	64 (71.11%)	

† **Fisher's exact test,** ‡ **Chi square test**

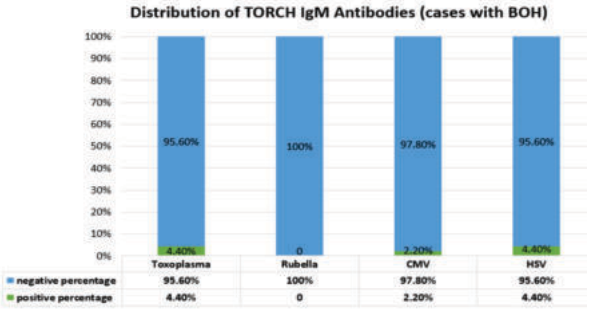

Figure 2: Distribution of TORCH IgM Antibodies (cases with BOH)

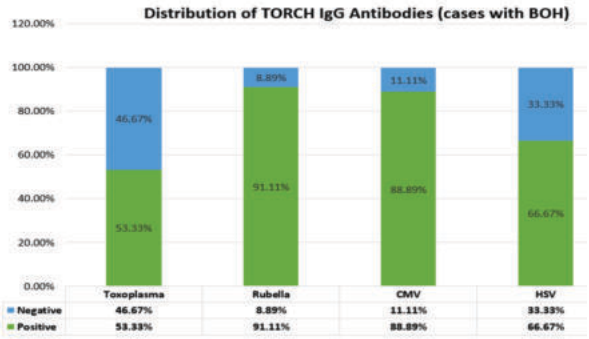

Figure 3: Distribution of TORCH IgG antibodies (cases with BOH).

As depicted in Table 2, majority of our study subjects did not have a history of Consanguinity (70; 77.78%), whereas a few participants did report history of consanguinity (20; 22.22%). There was a statistically significant difference ($p<0.05$) when consanguinity was compared in participants with good and bad obstetric history. Consanguinity was more prominent in participants with bad obstetric history (14; 31.11%) as compared to participants with good obstetric history (6; 13.33%).

Table 2: Comparison of consanguinity between good and bad obstetric history.

Consanguinity	Good obstetric history(n=45)	Bad obstetric history(n=45)	Total	P value
No	39 (86.67%)	31 (68.89%)	70 (77.78%)	0.043‡
Yes	6 (13.33%)	14 (31.11%)	20 (22.22%)	
Total	45 (100%)	45 (100%)	90 (100%)	

As depicted in Table 3, distribution of bad obstetric history parameters majority of our study subjects had a history of two or more abortions (40; 44.44%) followed by intra uterine growth retardation (2; 2.22%) and still birth (2; 2.22%) and least with history of intra uterine death (1; 1.11%). We could not find any participants with history of malformations or any other bad obstetric history parameters. There was a statistically significant difference ($p<0.05$) when comparison of bad obstetric history was made between participants with good and bad obstetric history in terms of abortion. There was no statistically significant difference in terms of other parameters (IUGR, still birth, Malformation, IUD, or any other).

Table 3: Comparison of BOH parameters between good and bad obstetric history.

Bad obstetric history parameters	Good obstetric history(n=45)	Bad obstetric history(n=45)	Total	P value
Abortion	0 (0%)	40 (88.88%)	40 (44.44%)	<.0001†

IUGR	0 (0%)	2 (4.44%)	2 (2.22%)	0.494†
Still birth	0 (0%)	2 (4.44%)	2 (2.22%)	0.494†
Malformation	0 (0%)	0 (0%)	0 (0%)	No p value
IUD	0 (0%)	1 (2.22%)	1 (1.11%)	1†
Other	0 (0%)	0 (0%)	0 (0%)	No p value

As depicted in figure 4, there was no statistically significant difference (p>0.05) when comparison of number of concurrent infections in terms of IgG positivity was made in participants with good and bad obstetric history. Majority of participants had 3 concurrent infections (39; 43.33%), followed by 4 concurrent infections (32; 35.56%), and with 2 concurrent infections (12; 13.33%).

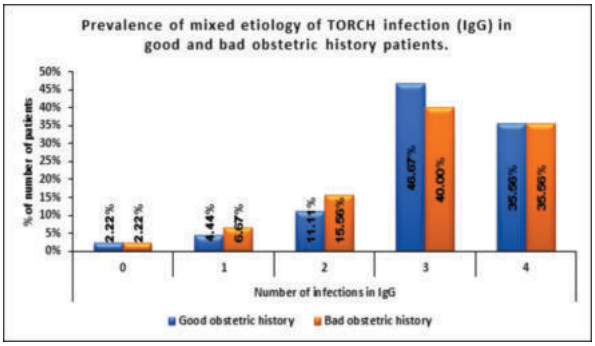

Figure 4: Prevalence of mixed etiology of TORCH infection (IgG) in good and bad obstetric history patients.

As depicted in table 4, there was no statistically significant difference (p>0.05) when comparison of number of concurrent infections in terms of IgM positivity was made in participants with good and BOH patients. We could not find any concurrent TORCH infections in terms of IgM positivity.

Table 4: - Prevalence of mixed etiology of TORCH infection (IgM) in good and bad obstetric history patients.

Co-infections (IgM)	Good obstetric history(n=45)	Bad obstetric history(n=45)	Total	P value
No infection	45 (100%)	40 (88.88%)	85 (94.44%)	0.242 †
Only Mono infected	0 (0%)	5 (11.11%)	5 (5.55%)	
Total	45 (100%)	45 (100%)	90 (100%)	

DISCUSSION

Maternal infections play a critical role in pregnancy wastage and their occurrence in patients with BOH or complicated pregnancy is a significant risk factor. One of the contributors to early and late childhood morbidity are the viral pathogens which crosses the placenta.[7] Detection of Toxoplasma, Rubella, Cytomegalovirus and Herpes Simplex Virus during pregnancy is important to prevent various manifestations which could occur in neonates by these agents. Value of screening is a subject to debate in various countries as various factors affect prevalence like geographical, socioeconomic and cultural conditions.[8]

In the present study, total IgM seropositivity of TORCH (including BOH cases and control group) infections was found to be 5.55%. Similarly, a study was done by Acharya R in 2020 reported the seroprevalence of 4.8%.[9] Unlike our study higher prevalence 13.8%, 37.9%, 98.8% was found in studies by Padmavathy M et al., Rajani M et al., Nirmal K et al.[7,10,2]

The total IgG seroprevalence of TORCH infections (including BOH cases and control group) was found to be 76.11%.

In this study, out of 45 pregnant women with BOH, a total of 2 (4.4%) were positive for IgM Toxoplasma. CMV IgM positive were 1 (2.2.%) and HSV IgM positive were 2 (4.4%). We did not find any samples positive for Rubella IgM and Syphilis antibodies. Similar to our study low prevalence rates of IgM TORCH positive in females with BOH were found in other studies by Sadik MS et al., Kumar R et al., Sahu SK et al., Padmavathy M et al. and Prasoona KR et al.[11,12,5,7,13] Unlike our study higher prevalence rates of TORCH IgM were found in studies such as Turbadkar D et al. and Manjunathachar H et al.[14,15]

The IgG Antibodies for Toxoplasma were positive in 24(53.3%) cases. Rubella IgG positive were 41(91.1%), CMV IgG positive were 40(88.8%) and HSV IgG positive were 30 (66.6%). These finding were similar to findings of Kumar R et al., Manjunathachar H et al., Sahu SK et al. and Prasoona KR et al. who also found high prevalence of IgG Positive TORCH infections in women with BOH. [12,15,5,13] Unlike our study Sadik MS et al found lower prevalence of IgG positive TORCH infections in women with BOH.[11]

The prevalence of Toxoplasmosis has been linked to several factors such as different climates in different regions and rural or urban settings. In terms of Rubella our study revealed the IgG prevalence was very high as compared to IgM. Through the IgG estimation, our study has shown that maximum proportion of the tested patients have been pre exposed and acquired resistance to Rubella virus, which is in agreement with other study by Kaur K et al.[16]

It was observed that the seroprevalence of TORCH infections was more common in 21-30 years age group. This finding is analogous with studies done by Kumar R et al. from Rajasthan wherein they found, the maximum number of cases (86.6%) lied in the age group 21-30 years followed by (10.4%) in >30 years age group; Study by Rajani M et al. also found maximum TORCH positive cases (74.2%) in 21-30 years of age group followed by 23.5% in >30 years age group; probably because this is the most common child bearing age group.[12,10] Studies reported by Parikh J et al. and Gumber S et al. also found maximum number of seropositive cases in 21-30 years of age groups.[17,18]

In our study majority of BOH cases (41/45) were of Recurrent Abortions which accounted for all IgM Positive TORCH cases. There were 2 cases of IUGR and Still birth each and 1 case of IUD none of which were found positive for IgM antibodies for TORCH infections. Similar to our study, Kumar R et al. from Rajasthan reported that majority of participants 53.33% had two or more abortions, 21.33% had intrauterine deaths and around 10.66% had intrauterine growth retardation.[12] Other studies done by Das M et al. and Suryawanshi R et al. reported 38%, 9%, 20% and 51%, 36%, 27% cases of abortions, intrauterine deaths, and intrauterine growth retardation respectively.[19,20] In this study we found seroprevalence of IgM maximum in patients with two or more abortions, likewise in study by Nellimarla K, Surpam RB and Tiwari S et al. maximum seropositivity was found in patients who had history of spontaneous abortions.[1,4,6]

Similarly, there was no statistically significant difference (p>0.05) when comparison of number of concurrent infections in terms of IgM seropositivity was made in participants with good and bad obstetric history. We could not find any concurrent TORCH infections in terms of IgM positivity.

CONCLUSION

- The study concludes that as more than 50% of the study population depicted presence of TORCH IgG antibodies, it is emphasized that all antenatal women should be screened for presence of TORCH infection in the beginning of pregnancy itself.
- The variation in the percentage of seropositivity to IgM and IgG, IgM alone and IgG alone indicative of incidence and prevalence of TORCH infections reported by various

authors from India and abroad may be likely due to difference in geographical and socioeconomic conditions.

- New approaches for prevention and treatment of congenital TORCH infection are necessary, including antiviral interventions and the development of vaccine strategy.
- A sound knowledge of congenital and perinatal infections is essential for prompt recognition and management of these conditions in order to prevent further disease and disability.
- Also, an extensive study covering a large population should be conducted at a community level to know the seropositivity of TORCH agents and to know the real status of these infections in BOH cases.

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